

## REMARKS

### Introduction

As of the date of the Office Action of July 28, 2005, Claims 32-83 of the present application were under consideration. Claims 32-83 have been rejected as discussed in the following remarks.

### Cancellation of Claims

Claims 33, 35, 36, 45, 47, 48, 57, 59, 60, 71, 72, 76, 77, 81, and 82 are herein cancelled without prejudice or disclaimer. Applicant reserves the right to file continuing applications for the subject matter of the cancelled claims.

### Claim Objections

Claim 82 is objected to under 37 C.F.R. § 1.75(c) as being in improper dependent form for failing to further limit the subject matter of Claim 48. Claim 82 has been cancelled. Claim 56 is currently amended in accordance with the Examiner's suggestion. Applicant appreciates Examiner's assistance with this correction.

### Claim Rejections Under 35 U.S.C. § 112

Claims 33, 45 and 57 are rejected as being purportedly indefinite because they refer to a "cell wall" as a "membrane." These claims have been cancelled.

Claims 39, 41, 43, 51, 53, 55, 63, and 68 are rejected as being purportedly indefinite because they recite "said member" without proper antecedent basis. These claims have been amended. A proper antecedent basis is established in the claims as currently amended.

Claim 65 is rejected as indefinite because it recites "said capillary" without antecedent basis. Claims 71-73, 75-78, and 80-83 are rejected as indefinite because they recite "[t]he microinjection method" without antecedent basis. Claim 70 is rejected as indefinite because it recites "said substance to be injected" without antecedent basis. Claim 73 is rejected as

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indefinite because it recites "the substance to be injected" without antecedent basis. Claims 78 and 83 are rejected as indefinite because they recite "the capillary" without antecedent basis. Claim 80 is rejected as indefinite because it recites "said substance to be injected" without antecedent basis. Applicant believes that all of the above-listed rejections are the result of numbering errors in the claim references of the claims as submitted in the preliminary amendment of July 8, 2002. These errors have been corrected and a proper antecedent basis is now established for each claim. Claim 83 has been cancelled.

Written description requirement under 35 U.S.C. § 112, first paragraph

Claims 32-83 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner states that "[t]he specification fails to reduce to practice or disclose any specific combination, other than photosensitizing compounds plus light stimulation for perforation of lipid bilayers, that meets these functional criteria." (Official Action, page 5, lines 5-10.) Claims 32-83 have been amended to recite one embodiment including the combination of a membrane-denaturing substance and a stimulus where the membrane denaturing substance is either a photosensitizer or photocatalyst and the stimulus is light. As the Examiner admits this combination is reduced to practice and disclosed in the specification (see Official Action, page 6, lines 5-8), applicant respectfully requests that the Examiner's rejection of Claims 32-83 under the written description requirement of 35 U.S.C. § 112, first paragraph, be withdrawn.

Enablement requirement under 35 U.S.C. § 112, first paragraph

Claims 32-83 are rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the enablement requirement. The Examiner states that "the specification, **while being enabling for a method of denaturing or perforating a lipid membrane using a photosensitizing compound and light stimulation**, does not reasonably provide enablement for

the full scope of contemplated combinations of compounds and specific stimulations to denature/perforate a membrane, and does not reasonably provide enablement for methods of perforating cell walls or non-lipid membranes." (Official Action, pages 7-8, emphasis added.) As the claims currently recite the methods which the Examiner has stated are enabled by the specification, applicant requests that the Examiner's rejection of Claims 32-83 under the enablement requirement of 35 U.S.C. § 112, first paragraph, be withdrawn.

#### Double Patenting

Claims 56-60 and 79 are rejected under obviousness-type double patenting as being unpatentable over Claims 1 and 2 of U.S. Patent No. 6,753,171 ("the '171 Patent"). Applicant respectfully traverses this rejection.

For an obviousness-type double patenting rejection to be appropriate, a claim in the application must define an invention that is "merely an obvious variation of an invention claimed in the patent." M.P.E.P. § 804. "Any obviousness-type double patenting rejection should make clear: (A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue would have been an obvious variation of the invention defined in a claim in the patent." M.P.E.P. § 804.

Neither Claim 1 nor 2 of the '171 Patent recite or suggest the stimulus-carrying member recited in current Claims 56-60 and 79. Likewise, neither Claim 1 nor 2 of the '171 Patent recite or suggest local introduction of a stimulus by a stimulus-carrying member to a selected site on a membrane, as recited in the current claims. The Examiner refers to the '171 Patent specification and states that "a stimulus carrying member such as a microscope or other light source can be used to provide the light stimulus to the locale of the membrane-disrupting agent." (Official Action, page 11.) However, there is no suggestion in the claims or specification of the '171

Patent that the referred-to microscope is a stimulus-carrying member in that there is no suggestion the microscope carries the light stimulus from the light source, an argon ion laser, to the target cell. Rather, the laser is equipped within the microscope and the light is carried through space. Light exposure is limited to a single cell by targeting of the laser. (See the '171 Patent specification, column 15, lines 28-32.)

Not only is there no suggestion of the currently-claimed stimulus-carrying member in the '171 Patent, the section of the '171 Patent specification cited by the Examiner specifically refutes the suggestion of local introduction of light to the area of the target cell: "Since the excitation light has to pass through the plastic of the collagen-coated dish before reaching the cells, there is a necessity to consider light reduction." (The '171 Patent, column 15, lines 32-35.) Further, the Examiner provides no reasons why a person of ordinary skill in the art would conclude that the invention defined in the current claims would have been an obvious variation of the invention recited in Claims 1 and 2 of the '171 Patent. For the above reasons, applicant submits that current Claims 56-60 and 79 are not merely obvious variations of the invention in Claims 1 and 2 of the '171 Patent and, for that reason, requests that the double patenting rejection be withdrawn.

Applicant respectfully disagrees that Claims 56-60 and 79 are directed to an invention not patentably distinct from Claims 1 and 2 of the commonly assigned '171 patent for the reasons stated above. While maintaining this objection, applicant states that the conflicting inventions were commonly owned at the time the invention in the current application was made. Applicant requests that any rejection under 35 U.S.C. § 103(a) be precluded under § 103(c) on this basis.

Claim rejections under 35 U.S.C. § 102

Claims 32-33, 37-39, 44-46, 49-51, 65-58, 61-63, 69, 70, 73, 74, 79, and 83 are rejected under 35 U.S.C. § 102 as being anticipated by Bataille et al. (J. Cell. Biol. 111:1571-1582, 1990).

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The Examiner states of Bataille: "To the extent the needle pierces the membranes, the membranes are denatured, and the needle is considered to be a membrane-destroying substance. The needle is also considered to be a membrane destroying member and a capillary." (Official Action, page 13). Applicant disagrees with the Examiner as to the teachings of the Bataille patent. Bataille teaches microinjection of an oocyte nucleus using the physical force of a needle.

For a reference to be anticipatory, the reference must exactly describe each and every element of the claims. In contrast to Bataille, the claims, as currently amended, recite a membrane-denaturing substance including a photosensitizer or a photocatalyst. Neither a photosensitizer nor a photocatalyst is anticipated or suggested by a needle as disclosed by Bataille. A membrane-denaturing substance is recited in the current claims as examined and as amended, not a membrane-destroying substance. As the cited claims are not anticipated by Bataille based on the distinction between the membrane-denaturing substance and a needle, the ability of Bataille's needle to function as a membrane destroying member and/or a capillary is not relevant. The Examiner also states that "the required stimulus is the physical contact provided by forcing the needle through the membranes." (Official Action, page 13.) As currently amended, the claims recite the stimulus to light. Thus, physical contact as taught by Bataille does not anticipate or suggest the stimulus element currently recited.

The Examiner rejects Claims 79 and 83 as anticipated by Bataille on the basis that the claims "require injection of a substance 'into the membrane'" but that "the specification at page 10, lines 6 and 7, depicts Fig. 2 as a process of injecting a tip of a capillary 'into' a cell membrane, whereas inspection of Fig. 2 shows that the capillary is clearly punched through the membrane resulting in injection of a substance into the cell, inside the membrane." (Official Action, pages 13-14.) As currently amended, the cited claims limit the membrane-denaturing substance to a photosensitizer or a photocatalyst and the stimulus to light, as discussed in the

preceding paragraph. Thus, neither Claims 79 nor 83 are anticipated or suggested by Bataille. For the sake of clarity, both of these claims have been amended to replace injecting a desired substance into the membrane with injecting a desired substance inside the membrane. Because Bataille neither anticipates or suggests a membrane-denaturing substance nor a stimulus as currently described, applicant requests that rejection of the cited claims as being anticipated under § 102 by Bataille be withdrawn.

Claims 32-33, 37-39, 44-46, 49-51, 56-58, 61-63, 69, 70, 73, 74, 79, and 83 are rejected under 35 U.S.C. § 102 as being anticipated by Laffafian et al. (Biophys. J. 75:2558-2563, 1998). The Examiner states "to the extent that the needle modifies the membranes, the membranes are denatured, and the needle is considered to be a membrane-destroying substance. The needle is also considered to be a membrane destroying member, and a capillary." (Official Action, page 14.) Applicant disagrees with the Examiner as to the teachings of the Laffafian patent. Laffafian teaches microinjection of an neutrophil nucleus using a lipid-coated micropipette. For a reference to be anticipatory, the reference must exactly describe each and every element of the claims. In contrast to the Laffafian patent, the currently amended claims do not depend on modification by a needle to perforate a membrane. Rather, the currently amended claims recite a membrane-denaturing substance including a photosensitizer or a photocatalyst. Neither a photosensitizer nor a photocatalyst is anticipated or suggested by a needle as disclosed by Laffafian. A membrane-denaturing substance is recited in the current claims as examined and as amended, not a membrane-destroying substance. As the current claims are not anticipated by Laffafian based on the distinction between the currently claimed membrane-denaturing substance and Laffafian's needle, the ability of a needle to function as a membrane destroying member and/or a capillary is not relevant. The Examiner also states that "the required stimulus is the physical contact provided by forcing the needle into the membrane." (Official Action, page 14.)

As currently amended, the claims recite the stimulus to light. Thus, the physical contact taught by Laffafian does not anticipate or suggest the stimulus element as currently recited.

The Examiner also states that "certain claims including Claims 79 and 83 require injection of a substance 'into the membrane.' This limitation is met by the deposition into the cell membrane of the lipids that coat the needle." (Official Action, pages 14-15.) The cited claims, as currently amended, recite the membrane-denaturing substance is a photosensitizer or a photocatalyst and the stimulus is light, as discussed in the preceding paragraph. Accordingly, neither Claims 79 nor 83 are anticipated or suggested by Laffafian regardless of the above-mentioned limitation. For these reasons, applicant requests that rejection of the cited claims as being anticipated under § 102 by Laffafian be withdrawn.

Claims 32-39, 44-51, 66, 69-74, and 79-82 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chen et al. (U.S. Patent No. 5,445,608) as evidenced by Hale (U.S. Patent No. 5,089,384) and Morgan et al. (U.S. Patent No. 5,446,157). Applicant respectfully objects to the Examiner's combining of multiple references as the basis for a § 102(b) rejection and traverses this rejection. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "Normally, only one reference should be used in making a rejection under 35 U.S.C. 102." M.P.E.P. § 2131.01. According to this section of the M.P.E.P., the only exceptions to this rule are when the additional reference(s) are cited to: a) prove the primary reference contains an "enabled disclosure"; b) explain the meaning of a term used in the primary reference; or c) show that a characteristic not disclosed in the reference is inherent.

The Examiner's reliance on Chen "as evidenced by Hale and Morgan et al." does not fall under any of these exceptions. Chen teaches using light developed by an implantable probe to

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"illuminate a treatment site that has been perfused with a photoreactive agent" specifically for the purpose of destroying cells. (Chen, column 1, lines 21-26.) Chen neither expressly nor inherently describes each and every element of the cited claims. As an illustrative example, Chen does not describe perforating a membrane with a membrane-destroying member where perforation of the membrane recovers to the state prior to perforation, as recited in all of the cited claims. The Examiner does not cite Hale and/or Morgan to prove that Chen contains an "enabled disclosure," to explain the meaning of a term used in Chen, nor to show that a characteristic not disclosed in Chen is inherent. Thus, citation to Hale and Morgan is inappropriate and, for the above reasons, Chen fails to anticipate or suggest any of the cited claims. For these reasons, Applicant requests the rejection of the cited claims as being anticipated under § 102 by Chen as evidenced by Hale and Morgan be withdrawn.

Furthermore, the cited claims are not rendered obvious over Chen, either alone or in combination with either Hale or Morgan. There is no suggestion or motivation to combine or to modify Chen with either Hale or Morgan. Moreover, even if the references are combined, the combination of the references does not teach or suggest all the claim elements.

#### Claim Rejections under 35 U.S.C. § 103(a)

Claims 56-60 and 79 are rejected under the nonobviousness requirement of 35 U.S.C. § 103(a) over the '171 Patent.

A *prima facie* case of obviousness requires either a suggestion or motivation to combine references or to modify a reference, a reasonable expectation of success, and all the claim elements must be taught or suggested by the prior art references.

Applicant respectfully traverses this rejection on the same basis as set forth under the Double Patenting section of this Response and, for the reasons stated in that section, requests that this rejection be withdrawn.

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#### Conclusion

In view of the foregoing amendments and remarks, applicant respectfully submits that all claims are in condition for allowance. An early Notice of Allowance is respectfully requested. If the Examiner has any questions, the Examiner is invited to contact applicant's attorney at the number provided below.

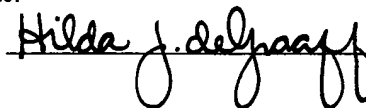
Respectfully submitted,

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Date: November 28, 2005



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